Research Article

Natural History of Vertically Transmitted Hepatitis C Virus

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Abstract

Background: Hepatitis C Virus (HCV) is an endemic disease with chronic sequelae that include cirrhosis and liver cancer. Children acquire the disease mainly via the maternal-infant route. This study investigated its prevalence in pregnant women and the natural history of its vertical transmission.

Methods: This prospective study involved 618 randomly selected pregnant women in Al-Ain City (Abu Dhabi, UAE). Participants were screened in the first trimester by second-generation Enzyme-Linked Immunosorbent Assays (ELISA-2). Positive samples were further tested by third-generation ELISA (ELISA-3), third-generation recombinant immunoblot assay for detection of antibodies (anti-HCV), and Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR) to detect HCV-RNA. Infants of mothers with positive anti-HCV antibody or HCV-RNA were followed for several years.

Results: Twenty-five women (4.0%) had positive ELISA-2; of which eleven (1.8%) had positive ELISA-3, nine (1.5%) had positive anti-HCV antibody, and three (0.5%) had positive HCV-RNA. All nine infants of mothers with positive anti-HCV antibody had positive anti-HCV antibody at 1, 6, and 12 months of age. All three infants of mothers with positive HCV-RNA had positive HCV-RNA and elevated Alanine Transaminase (ALT) for several years. All six infants of mothers with negative HCV-RNA had negative HCV-RNA and normal ALT at 1, 6, and 12 months of age.

Conclusion: The prevalence of positive anti-HCV antibody in infants of mothers with positive anti-HCV antibody was 9/9 at 12 months. The prevalence of HCV infection (positive HCV-RNA) among mothers in our region is about 0.5%. The prevalence of positive HCV-RNA in infants of mothers with positive HCV-RNA was 3/3 and of mothers with negative HCV-RNA 0/6 (p=0.012). These results justify long-term monitoring of infants born to mothers with positive anti-HCV or HCV-RNA.

Introduction

Hepatitis C virus (HCV) is a major cause of acute and chronic hepatitis worldwide. The World Health Organization estimated 170 million individuals are infected with HCV. Its prevalence, however, varies among different countries, with a large number of reported cases from Egypt due to the use of contaminated parenteral anti-schistosomal therapy [1-2].

About 3% of the world’s population is infected with HCV, with the highest prevalence occurring between 30 and 49 years of age [1]. In the United Arab Emirates (UAE), the prevalence of HCV among blood donors of 26 to 45 years of age is 1.7% and of those less than 25 years of age is 0% [3].

Sixty percent of patients with acute HCV infection become chronic carriers, predisposing them to serious liver diseases. Cirrhosis occurs in about 20% of infected patients. Up to 20% of patients with cirrhosis develop liver cancer [4]. With the current blood screening programs that ceased transfusion-associated HCV infection, children acquire the disease mainly via the maternal-infant route [5].

Mother-to-infant HCV transmission is well documented [4]. Nevertheless, limited data are available in highly diverse cultures, such as the UAE. This report describes: (1) the prevalence of HCV among pregnant women and (2) the outcome of its vertical transmission in Al-Ain Medical District (Abu Dhabi, UAE).

Methods

The study participants had attended prenatal care in Al-Ain Medical Districts between June 2001 and June 2002. Seven hundred randomly selected mothers (representing about 10% of total deliveries) were approached. Six hundred eighty (88%) mothers consented to the study; 104 (16.8%) mothers were UAE citizens and 514 (83.2%) were UAE residents (expatriates) from the Middle East, Indian sub-continent and Africa. Maternal data included transfusion history, parity, mode of delivery and breast feeding. HIV antibody and hepatitis B surface antigen were performed for routine antenatal care and were negative in all participants. Inclusion criteria were all pregnant...
women who consented to the study. Exclusion criteria were women who refused to participate in the study.

Consented mothers were screened in their first trimester by second-generation ELISA (ELISA-2; UBI HCV EIA 4.0, done in duplicates in the Department of Microbiology, College of Medicine and Health Sciences - UAE University). Positive serology was confirmed by third-generation ELISA (ELISA-3, BioElisa HCV of Biokit, S.A. Barcelona HCV - Bio Barcelona, Spain). Mothers with positive ELISA-3 had anti-HCV antibody immunoblot assay (anti-HCV, Bioblot HCV - Bio Kit Barcelona, Spain) and RT-PCR for HCV-RNA. A positive HCV-RNA indicated the presence of 272 and 256 base pair band PCR products. All procedures and interpretations were performed according to the manufacturers’ instructions.

Infants born to mothers with positive anti-HCV antibody were investigated by anti-HCV assay, HCV-RNA PCR and serum ALT (upper limit normal, 40 IU/L) >12 months of age. Mothers and infants were considered HCV-infected if HCV-RNA was positive.

The study was approved by the Committee for Protection of Human Subjects of the University of Texas Health Science Center at Houston and Al-Ain Medical District Human Research Ethics Committee and Federal Ministry of Health. A written informed consent was obtained for each participant. The data were analyzed using SPSS (v11.5).

Results
Six hundred eighteen mothers were screened by ELISA-2; 25 (4.0%) women were tested positive and underwent further investigation. Eleven (1.8%) women had positive ELISA-3, nine (1.5%) had positive anti-HCV, and three (0.5%) had positive HCV-RNA. Mothers with positive HCV-RNA were considered infected.

Infants of mothers with positive anti-HCV were monitored until at least 12 months of age. All infants had anti-HCV testing at one month of age. The three infants of mothers with positive HCV-RNA all had positive HCV-RNA, positive anti-HCV antibody, and elevated ALT for at least 12 months of age. These infants, considered HCV-infected, were singleton births with term deliveries. One of the infants was delivered by C-section for transverse position.

Discussion
In this study cohort, nine (1.5%) mothers had anti-HCV antibody and three (0.5%) had HCV-RNA. The three infants of mothers with HCV-RNA had positive HCV-RNA for >12 months. The six infants of mothers without HCV-RNA had negative HCV-RNA at 12 months. Thus, the vertical transmission in HCV-RNA negative mothers was 0/6 and in HCV-RNA positive mothers was 3/3 (p=0.012; Fisher’s exact test).

The representative profile for infant #1 is shown in (Table 1). This infant girl had positive HCV-RNA at 1, 8, 13, 27, 42, and 59 months of age. Her anti-HCV antibody was also consistently positive up to 15 years of age along with evidence of liver disease marked by markedly elevated ALT at 42 months of age. For Family #2, high viral titer in the first trimester. Her infant also had a high viral titer and positive HCV-RNA had positive HCV-RNA for >12 months. The six infants of mothers without HCV-RNA had negative HCV-RNA at 12 months. Thus, infants of mothers with HCV-RNA need treatment and long-term monitoring. The results also advocate for screening high-risk pregnant women for HCV-RNA, since the impact of this disease on the children is substantial.

As shown in Table 1, the mother of Family #1 had high HCV-RNA titer in the first trimester. Her infant also had a high viral titer and markedly elevated ALT at 42 months of age. For Family #2, high viral titer was present at 15 years of age along with evidence of liver disease (Table 2). Therefore, long-term monitoring and anti-viral treatment of these patients are warranted.

Recent epidemiology of HCV and HBV in the UAE is summarized in (Tables 4-5). The frequency of both infections increases with age, which reflects accumulative risks of the viral exposure (Table 4). Consistently, the prevalence of HCV in our premarital screening program (Table 5) is similar to that found in our study (about 0.5%).

Table 4: HCV and HBV cases notified in Abu Dhabi (2010-2012).

<table>
<thead>
<tr>
<th>Year</th>
<th>Age (y)</th>
<th>HCV</th>
<th>HBV</th>
</tr>
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<tr>
<td>2010</td>
<td>&lt;1</td>
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<td>2</td>
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<tr>
<td></td>
<td>1 to &lt;5</td>
<td>2</td>
<td>3</td>
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<td>5 to &lt;10</td>
<td>12</td>
<td>22</td>
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In conclusion, this study shows the prevalence of HCV-RNA among pregnant women is about 0.5%. The frequency of mother-to-infant vertically transmission is 100%. The infection in infants is chronic and causes long-term sequelae. Treatment of HCV is available and effective. Therefore, screening mothers and infants for HCV-RNA is advisable, especially in high risk populations (e.g., people who received contaminated parenteral anti-schistosomal therapy) [12-14].

Acknowledgement

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References